

Comments on "Length scale dependence of DNA mechanical properties"

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In a recent paper by Noy and Golestanian [1] (NG) the elastic properties of DNA were studied by molecular dynamics (MD) simulations. Two important conclusions were made: (i) the computed bending and twisting rigidities of DNA agree well with experimental data, and (ii) for lengths of a few helical turns, DNA dynamics exhibits long-range correlations in qualitative difference from the worm-like rod (WLR) model. Earlier similar studies showed that (i) the current MD forcefields systematically overestimate the DNA rigidity, and (ii) MD trajectories of DNA involve only short-range correlations; no deviations from the WLR model are detectable if MD data are analyzed properly. Here it is argued that the data analysis in NG was not correct and that the earlier conclusions are valid.

The first note concerns ergodicity of MD sampling and statistical errors. This is a standard issue for such studies, but it was omitted in NG. In the most intensive earlier simulations the DNA rigidity was evaluated from 164 ns trajectories of one helical turn [2, 3]. This duration exceeded the measured relaxation times by about 3 orders of magnitude and provided the accuracy below 5% for the computed persistence lengths. NG analyzed 100 ns dynamics of 3 and 5 DNA turns and it was implied that by considering many internal stretches of long DNA one improves the sampling. However, this intuitive assertion is valid only for stretching. For bending and twisting the true gain in sampling is close to zero or even negative because the relaxation of a double helical fragment is slower when it is a stretch of longer DNA [4, 5]. In addition, the self-diffusion coefficient of SPCE water used in NG is two times smaller than that of TIP3P model in earlier studies. Overall, for one helical turn, the effective sampling volume in NG probably was several times smaller than before. For longer DNA the sampling was largely insufficient because the relaxation times for twisting and bending grow with the DNA length as L^2 and L^4 , respectively. For 5 turns this gives relaxation times comparable with and beyond 100 ns.

The second note concerns comparisons with the WLR model. The authors analyzed MD trajectories with methods that were never tested for WLR and there are strong reasons to believe that, in fact, the results would not be very different. Notably, the slowest stretching normal mode represents an accordion movement, with the whole WLR extending and shrinking concertedly. This mode

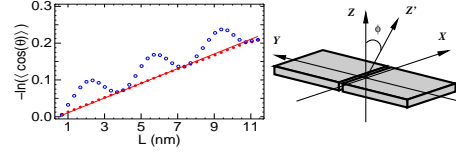


FIG. 1: Color online. Length dependence of the bend angle θ for Brownian dynamics of a WLR [5]. The same trajectory was analyzed with angle θ measured between either true Z-vectors (closed red circles) or biased Z'-vectors (open blue circles) shown on the right. The bias angle $\phi = 10^\circ$. The straight red line shows the theoretical dependence.

can be extracted using the principal component analysis, and superposition of representative structures would give a pattern similar to that shown in NG, but it is not a sign of real correlations. The bending contribution to the end-to-end distance is accumulated through the whole contour length and it is only partially eliminated by using covariances measured between the terminal base pairs. Finally, oscillations with the helical period observed in some plots are inevitably produced by the algorithm used for constructing reference base-pair frames. This algorithm yields Cartesian frames that fit the global helical axis in an early ideal B-DNA model. For MD structures such frames are systematically biased. When this feature is taken into account for WLR it produces periodical patterns similar to those shown in NG (see Fig. 1). This is the main source of spurious oscillations in MD data [6], but it is an artifact rather than an evidence of correlations and deviations from the WLR model.

In summary, all-atom MD simulations with the current AMBER forcefield somewhat overestimate the bending and twisting rigidities of the double helix. MD simulations agree well with the WLR model, with no detectable correlations beyond a few base pair steps. However, for non-integral number of helical turns the data analysis requires special care [5, 6]. Therefore, additional work is necessary for improving both the MD forcefields and interpretations of experimental data.

[1] A. Noy and R. Golestanian, Phys. Rev. Lett. **109**, 228101 (2012).

- [2] A. K. Mazur, Phys. Rev. Lett. **105**, 018102 (2010).
- [3] A. K. Mazur, Phys. Rev. E **84**, 021903 (2011).
- [4] A. K. Mazur, J. Phys. Chem. B **112**, 4975 (2008).
- [5] A. K. Mazur, J. Phys. Chem. B **113**, 2077 (2009).
- [6] A. K. Mazur, Biophys. J. **91**, 4507 (2006).